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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/781,296	01/13/97	HARLEY J	OMRF161

HM21/0624

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EXAMINER	
ZEMAN, M	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 06/24/98

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	15

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 1/27/98 + 3/30/98

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire - 3 - month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-5 + 11-18 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-5 + 11-18 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 10
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

-SEE OFFICE ACTION ON THE FOLLOWING PAGES-

* U.S. GPO: 1996-421-632/40206

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1643.

2. Claims 1-5 and 11-18 are pending in this application. Applicants have elected group I, claims 1-5 and 11-18 in part (e.g. the polypeptide), along with the species of systemic lupus erythematosus, and SEQ ID NO: 1. The other groups, and species present in claims 1-5 and 11-18 have been withdrawn from consideration as being drawn to a non elected invention.

3. Applicant's election with traverse of Group I, claims 1-5 and 11-18 in part in Paper No. 10 and 12 is acknowledged. The traversal is on the ground(s) that claims 1-5 and 11-18 should be viewed as proper Markush claims wherein the vaccine is selected from DNA, peptides or carbohydrates. This is not found persuasive because each invention as set forth in the restriction requirement is a patentably distinct separate physiochemical entity. Compositions comprising DNA are quite different both chemically and biochemically from compositions comprising polypeptides, which are likewise quite different from compositions comprising carbohydrates. These compositions do not have similar properties or methods of action, nor do they all have the same purpose. Applicant asserts that "from their nature, the prior art and the application that embodiments of all three possess this property". This is not persuasive, as there is no evidence set forth in the specification that DNA or carbohydrates act in the same way as polypeptides, not has

Applicant pointed out prior art supporting this assertion. Furthermore, while there may be some relationship between a DNA and the polypeptide it encodes, there is no such potential relationship between unspecified carbohydrates and DNA or said carbohydrates and polypeptides. For the reasons set forth above, and the reasons set forth in the restriction requirement, the requirement is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to all of the prior application(s) in the first sentence of the specification (37 CFR 1.78) and must include the status of that application.

Information Disclosure Statement

5. The information disclosure statement filed 2/9/98 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The examiner has reviewed the parent applications of this application for the purposes of finding the references cited upon the information disclosure statement, however a copy of the each and

every listed reference was not found. The references considered have been initialed. If Applicant wishes the other references to be considered, a copy of said references and a PTO-1449 listing said references should be submitted. It is noted that Hardgrave et al, and Kaufman et al. do not list a publication year. The publication year of the references is required.

Claim Rejections - 35 USC § 112

6. Claims 1-5 and 11-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 11, and dependent claims thereon, set forth a vaccine and method of treating autoimmune disorders caused by EBV, wherein the composition and treatment comprise the administration of live unattenuated EBV. It is not clear how the administration of live unattenuated virus would prevent the development of disorders caused by that same virus.

The term "individual at risk" in claim 11 is a relative term which renders the claim indefinite. The term "at risk" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The risk factors to be assessed in the administration of the composition are not clearly set forth. Is the simple infection with EBV the only risk factor involved?

The term "symptoms associated with" in claim 11 is a relative term which renders the claim indefinite. The term "symptoms associated with an autoimmune disease" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant is claiming means of treating innumerable autoimmune diseases which have widely disparate (and in many cases non-overlapping) symptoms, such that it is impossible to determine what symptoms would identify a patient as needing the claimed compositions. Many of the symptoms of autoimmune diseases overlap with diseases not of autoimmune origin, and therefore would not necessarily be a relevant indicator for identification of suitable patients.

Claim 4 is rejected as it does not recite the sequence identification number of the relevant peptides sequences in the claims.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 11-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-5 are drawn to a vaccine composition which can "alleviate or prevent" autoimmune disorders. Claims 11-18 are drawn to methods of "preventing or alleviating"

autoimmune disorders. The vaccine comprises EBV or a component thereof. The elected species is a nuclear antigen 1 protein lacking the PPPGRRP epitope. The elected autoimmune disease is systemic lupus erythematosus (SLE).

The specification appears to be directed to the detection of EBV infection, and correlation of that detection with autoimmune diseases. The specification does not set forth the successful treatment, alleviation, or prevention of any autoimmune disease, or symptom thereof. The term "alleviation" refers to the lessening or cessation of the autoimmune disorder, or symptoms of that disorder. The term "prevention" means that the subject receiving the composition never develops the autoimmune disease or symptoms of that disease, even upon challenge with live unattenuated EBV.

The specification does not set forth any examples wherein the administration of the elected composition in an accepted animal model is able to successfully "alleviate" an already existing autoimmune disease. The specification does not set forth any examples wherein the administration of the elected composition totally or partially "prevents" the development of an autoimmune disorder in an accepted animal model. There are no experiments which challenge vaccinated animals with live unattenuated EBV such that the prevention of the autoimmune disease is shown.

The specification does not set forth any direct correlation between the administration of the elected composition, and the development/alleviation/prevention of the elected autoimmune disorder. While antibodies to a particular epitope could be common in a patient with SLE, there

is no indication that the administration of the entire protein, lacking that sequence would have any effect upon the clinical course of the disease, whether it be preventing the development of that disease, or the treatment of that disease. It is also not clear that the administration of the claimed composition would prevent the development of antibodies to the deleted region when challenged with native virus. If the epitope is such a strong SLE epitope, it is possible that despite the vaccine, the patient may develop antibodies to the PPPGRRP motif upon challenge with native virus. SLE patients have many "abnormal" antibodies present in their serum. (Abnormal in the sense that normal patients do not have antibodies to the same epitopes) It is presently not known whether the presence of the antibodies is the cause or the effect of the autoimmune disease; i.e. do the antibodies cause the symptoms of SLE, or does the course of SLE allow the development of abnormal antibodies.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The examiner has reviewed the parent applications 08/160,604, filed 11/30/93, 07/867,819 filed 4/13/92, and 07/472,947 filed 1/31/90. The examiner has also reviewed the provisional application 60/019,053 filed 5/16/96. The first application disclosing the administration of EBV or EBV components is the provisional application 60/019,053. Therefore, all of the pending claims are accorded the effective filing date of 5/16/96.

9. Claims 1, 2, 3, 5, 11, 12, 13 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Kieff.

Claim 1 is drawn to a vaccine composition comprising EBV, or components of EBV. Claims 2 and 3 further define acceptable components of the vaccine. Claim 5 sets forth the vaccine is injected. Claims 11, 12, 13 and 16 are drawn to methods of preventing disorders induced by infection with EBV, essentially protecting from infection with native virus. The composition administered in claims 11, 12, 13 and 16 is EBV or a component thereof.

Kieff (US Patent 4,707,358) sets forth vaccine compositions for EBV comprising an EBV polypeptide in an amount effective to prevent infection. The vaccine can be administered parenterally.

10. Claims 1, 2, 3, 5, 11, 12, 13 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Alderson.

Alderson (US Patent 5,726,286) sets forth vaccine composition for EBV comprising BZLF2 polypeptides, and methods of preventing infection with EBV. The vaccine compositions can be administered parenterally.

11. Claims 1, 2, 3, 5, 11, 12, 13 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Wolf.

Wolf (US Patent 5,679,774) discloses vaccine compositions comprising one or more EBV polypeptides, and methods of preventing infection with EBV. The vaccine compositions can be administered parenterally.

12. Claims 1-5, 11, 12, 13, 14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Vaughan.

Vaughan (US Patent 4,654,419) discloses vaccine compositions comprising one or more EBV nuclear antigen protein 1 polypeptides, and methods of preventing infection with EBV. The EBNA proteins do not have the PPPGRRP sequence. The vaccine compositions can be administered parenterally.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to

the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 14, 15, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vaughan as applied to claims 1-5, 11-13 and 16 above, in view of Harley.

Claims 14, 15, 17 and 18 are drawn to methods of vaccinating with a composition comprising an EBNA antigen lacking the PPPGRRP, wherein the disease to be treated or prevented is SLE.

Vaughan (US Patent 4,654,419) discloses vaccine compositions comprising one or more EBV nuclear antigen protein 1 polypeptides, and methods of preventing infection with EBV. The EBNA proteins do not have the PPPGRRP sequence. The vaccine compositions can be administered parenterally. Harley (Harley and James 1995 J Lab Clin Med 126 (6) 509-516) discusses the importance of EBNA specific antibodies in SLE, and suggests that antibodies to the PPPGRRP sequence may play a role in the disease etiology of SLE. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the compositions of Vaughan for the treatment of SLE, as the compositions of Vaughan do not have the PPPGRRP motif indicated in the development of SLE.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can be reached between the hours of 8:00 am and 5:30 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marian Knode, can be reached on (703) 308-4311.

The fax number for this Art Unit is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

mkz
June 18, 1998

ANTHONY C. CAPUTA
PRIMARY EXAMINER